

Appl. No. : 08/841,847  
Filed : May 5, 1997

### REMARKS

Claims 62, 66-76, 79-91, 94-126, 128, and 131-154 were pending in the above-referenced application. Claims 62, 109, and 123 have been amended. Claims 155-172 have been added and recite additional functional characteristics of the claimed invention. These amendments are supported by the specification and the originally filed claims. For example, support for the ratios recited in the claims presented above is found on page 19, lines 28-35, and in the original claims. Microbubble dimensions are discussed generally on page 19, lines 27-28. Gas mixtures opposing Laplace pressure *in vivo* is discussed on page 20, lines 5-23. Accordingly, the amendments proposed herein do not constitute new matter. Claims 62, 66-76, 79-91, 94-126, 128, and 131-172 are now presented for examination.

#### Interview

Applicants thank the Examiner for the courtesy shown during the telephonic interview of February 16, 2000. Participants in the interview were Examiner Hollinden, and Applicants' representatives Ned A. Israelsen and James J. Mullen III, Ph.D. No exhibits were shown and no demonstrations were conducted during the course of the interview. Claims 62, 66-76, 79-91, 94-126, 128, and 131-154 were discussed during the interview and agreement was not reached.

During the course of the interview Applicants' representatives suggested replacing the language regarding a "fixed molar ratio" with specific numerical ranges disclosed in the specification. It was noted that the prior art only teaches the general concept of mixtures and fails to disclose any specific amounts or ratios. Accordingly, the claiming of such specific ranges would clearly overcome the teachings of the prior art. Additional dependent claims reciting certain functional limitations concerning the properties of the claimed microbubbles after *in vivo* administration were also discussed.

#### Nonobviousness of Pending Claims

The United States Patent and Trademark Office (PTO) rejected claims 62, 66-76, 79-91, 94-126, 128, and 131-154, under 35 U.S.C. § 103 as being unpatentable over Lambert et al. (5,552,133), Quay (5,573,751), and Schneider et al. (5,413,774) for reasons of record stated in the previous Office Actions. Specifically, the PTO has argued that the art cited against claims 51-171 renders the invention disclosed therein obvious because the cited art teaches mixtures of

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gas osmotic agents and modifier gases. Applicants note that the filing date of the Lambert reference (August 12, 1994) is after the filing date of the parent of the present application (July 30, 1993) and therefore not a proper prior art reference. Notwithstanding the teachings of the cited art, the references listed above do not teach the particular ratios of gases now recited in the pending claims to obtain an osmotically stabilized microbubbles. Because the art fails to teach all the limitations of the claimed invention, the PTO has failed to articulate a prima facie case of obviousness.

The present case is analogous to the case of *In re Antonie*, in which the Board of Appeals was reversed for upholding an obviousness rejection of a wastewater treatment device. *In re Antonie*, 559 F.2d 618 (CCPA 1977). The court determined in *In re Antonie* that the invention related to a particular ratio which related directly to the treatment capacity of the device. *Id.* at 619. The art cited against the claims in that case taught similar design parameters, but did not teach the ratio used by the Applicant. The court held that the differences between the prior art and the pending claims were not obvious because the prior art did "not reveal the property which applicant has discovered," and the PTO has provided no other basis for the obviousness rejection. *Id.* at 620.

Just as in *In re Antonie*, the pending claims now presented for examination recite a particular ratio that distinguishes those claims from the prior art. The specification of the above-referenced application discloses the use of particular ratios of gases to achieve an osmotically stabilized microbubble preparation. The cited art does not teach, suggest, or otherwise disclose these claimed features. Furthermore, the mere recitation of gas mixtures, without specific teachings or suggestions to provide the gases in particular ratios to stabilize the resulting microbubbles, fails to render the pending claims obvious. In view of this deficiency, Applicants respectfully request withdrawal of the pending obviousness rejection and allowance of the pending claims.

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### CONCLUSION

Applicants believe that all issues raised in the previous Office Action have been addressed. Nevertheless, the Examiner is invited to telephone the undersigned attorney at the number below with any questions that may remain if it is believed that this will expedite prosecution of the present application.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR

Dated: 20 June 2000

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